In the claims:

Please amend the claims as follows:

1. (Currently Amended) An isolated nucleic acid molecule comprising at least [[24]] 34 contiguous ~~bases of nucleotide sequence first disclosed in the NHP polynucleotide described in~~ nucleotides from SEQ ID NO:1.

2. (Currently Amended) An isolated nucleic acid molecule comprising a nucleotide sequence that:

(a) encodes the amino acid sequence shown in SEQ ID NO:2; and

(b) hybridizes ~~under stringent conditions~~ to the nucleotide sequence of SEQ ID NO:1 or the complement thereof under highly stringent conditions of 0.5 M $NaHPO_4$, 7% sodium dodecyl sulfate (SDS) and 1 mM EDTA at 65°C and washing in 0.1x SSC/0.1%SDS at 68°C.

3. (Original) An isolated nucleic acid molecule encoding the amino acid sequence described in SEQ ID NO:2.

4. (New) The isolated nucleic acid molecule of claim 1, wherein said nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:1.

5. (New) A recombinant expression vector comprising the isolated nucleic acid molecule of claim 1.

6. (New) The recombinant expression vector of claim 5, wherein the isolated nucleic acid molecule encodes the amino acid sequence described in SEQ ID NO:2.

7. (New) The recombinant expression vector of claim 6, wherein the isolated nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:1.

8. (New) A host cell comprising the recombinant expression vector of claim 5.

RESPONSE

I. Status of the Claims

No claims have been cancelled. Claims 1 and 2 have been amended. New claims 4-8 have been added.

Claims 1-8 are therefore presently pending in the case.

II. Support for the Amended Specification and Amended and Newly Added Claims

The specification has been amended to include a title that does not include the term "novel". Support for the new title can be found in the original title, and throughout the specification and claims as originally filed.

Claim 1 has been amended to specifically recite an isolated nucleic acid molecule comprising at least 34 contiguous nucleotides from SEQ ID NO:1. Support for this claim can be found throughout the specification as originally filed, with particular support being found in claim 1 as originally filed, and at page 5, line 4.

Claim 2 has been revised to further clarify the claim by reciting specific highly stringent hybridization conditions. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least at page 4, lines 4-7.

Claim 4 has been added to specifically recite an isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1. Support for this claim can be found throughout the specification as originally filed, with particular support being found in claim 1 as originally filed.

Claims 5-7 have been added to specifically recite expression vectors comprising nucleic acid molecules of the present invention. Support for these claims can be found throughout the specification as originally filed, with particular support being found at least at page 13, lines 4-10.

Claim 8 has been added to specifically recite host cells comprising the expression vector of claim 5. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least at page 13, lines 10-16.

It will be understood that no new matter is included within the amended or newly added claims.

III. Title

The Action first objects to the title of the application for the use of the word "novel". Applicants have amended the title of the present application to remove the term "novel".

Applicants request that, since the objection has been overcome, this objection be withdrawn.

IV. Abstract

The Action next objects to the abstract of the application as being non-descriptive. Applicants point out that numerous issued U.S. Patents have an abstract **identical** to the present abstract. Specifically, Applicants direct the Examiner's attention to issued U.S. Patent Nos. 6,433,153, 6,441,153, 6,441,154, 6,444,456 and 6,448,388. As issued U.S. Patents are presumed to meet all necessary PTO requirements, Applicants submit that the present abstract must also meet all necessary PTO requirements.

Applicants request that, since the objection has been overcome, this objection be withdrawn.

V. Rejection of Claims 1-3 Under 35 U.S.C. § 101

The Action first rejects claims 1-3 under 35 U.S.C. § 101, as allegedly lacking a patentable utility. Applicants respectfully traverse.

The present invention has a number of substantial and credible utilities, not the least of which is in diagnostic tests, such as forensic analysis, as described in the specification, at least at page 10, lines 14-20. As described in the specification at page 15, lines 21-29, the present sequence defines two coding single nucleotide polymorphisms - specifically: a G/A polymorphism at nucleotide position number 68 of SEQ ID NO:1, which can result in an arginine or glutamine residue at amino acid position 23 of SEQ ID NO:2; and an A/G polymorphism at nucleotide position number 82 of SEQ ID NO:1, which can result in an alanine or threonine residue at amino acid position 28 of SEQ ID NO:2. As such polymorphisms are the basis for forensic analysis, which is undoubtedly a "real world" utility, the present sequences must in themselves be useful. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Applicants respectfully point out that the use of the presently described polymorphisms in forensic analysis does not require the identification of a specific medical condition. The presently described polymorphisms are useful in forensic analysis exactly as they are described in the specification as originally filed - specifically, to identify individual members of the human

population based on the presence or absence of one or more of the described polymorphisms. This is also not a case of a "potential" utility. Using the polymorphic markers exactly as described in the specification as originally field can definitely distinguish members of a population from one another. In the worst case scenario, each marker is useful to distinguish 50% of the population (in other words, a marker being present in half of the population). The ability to eliminate 50% of the population from a forensic analysis clearly is a real world, practical utility. Therefore, any allegation that the use of the presently described polymorphic markers is only potentially useful would be without merit, and would not support the alleged lack of utility.

The Examiner discounts this asserted utility, stating that this utility "is an application which (*sic*) would apply to every member of a general class of materials and/or is a use only for further research to determine a use for SEQ ID NO:1 or the protein encoded thereby" (Action bridging pages 2 and 3). Applicants first point out that not all nucleic acids contain polymorphic markers. In fact, the basis for forensic analysis is the fact that such polymorphic markers are not present in all other nucleic acids, but in fact specific and unique to only a certain subset of the population. Until a polymorphic marker is actually described it cannot be used in forensic analysis. Put another way, simply because there is a likelihood, even a significant likelihood, that a particular nucleic acid sequence will contain a polymorphism and thus be useful in forensic analysis, until such a polymorphism is actually identified and described, such a likelihood is meaningless. Second, the Examiner seems to be confusing the requirement for a **specific** utility, which is the proper standard for utility under 35 U.S.C. § 101, with the requirement for a **unique** utility, which is clearly an improper standard. As clearly set forth by the Federal Circuit in *Carl Zeiss Stiftung v. Renishaw PLC*, 20 USPQ2d 1101 (Fed. Cir. 1991):

> An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding a lack of utility." *Envirotech Corp. v. Al George, Inc.*, 221 USPQ 473, 480 (Fed. Cir. 1984)

Just because other, or even more useful, polymorphic sequences from the human genome have been described does not mean that the use of the presently described polymorphic markers for forensic analysis is not a specific utility. If every invention were required to have a unique utility, the Patent and Trademark Office would no longer be issuing patents on batteries, automobile tires, golf balls, golf clubs, and treatments for a variety of human diseases, such as cancer, just to name a few particular examples, because the utility of each of these compositions is applicable

to the broad class in which each of these compositions falls: all batteries have the same utility, specifically to provide electrical power; all automobile tires have the same utility, specifically for use on automobiles; all golf balls and golf clubs have the same utility, specifically for use in the game of golf; and all cancer treatments have the same utility, specifically, to treat cancer. However, only the briefest perusal of virtually any issue of the Official Gazette provides numerous examples of patents being granted on each of the above compositions nearly every week. Furthermore, if a composition needed to be unique to be patented, the entire class and subclass system would be an effort in futility, as the class and subclass system serves solely to group such common inventions, which would not be required if each invention needed to have a unique utility. Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

Furthermore, as the presently described polymorphisms are part of the family of polymorphisms that have a well established utility, the Federal Circuit's holding in *In re Brana,* (34 USPQ2d 1436 (Fed. Cir. 1995), "*Brana*") is directly on point. In *Brana*, the Federal Circuit admonished the Patent and Trademark Office for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442. The Federal Circuit went on to state:

> At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant provide regarding the practical utility or usefulness of the invention for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago.

Brana at 1439, emphasis added. The choice of the phrase "utility or usefulness" in the foregoing quotation is highly pertinent. The Federal Circuit is evidently using "utility" to refer to rejections under 35 U.S.C. § 101, and is using "usefulness" to refer to rejections under 35 U.S.C. § 112, first paragraph. This is made evident in the continuing text in *Brana*, which explains the correlation between 35 U.S.C. §§ 101 and 112, first paragraph. The Federal Circuit concluded:

> FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

Brana at 1442-1443, citations omitted, emphasis added. As set forth above, the present

polymorphisms are useful in forensic analysis exactly as they were described in the specification as originally filed, without the need for any further research. Even if the use of these polymorphic markers provided additional information on the percentage of particular subpopulations that contain these polymorphic markers, this would not mean that "additional research" is needed in order for these markers as they are presently described in the instant specification to be of use to forensic science. As stated above, using the polymorphic markers as described in the specification as originally field can definitely distinguish members of a population from one another. However, even if, *arguendo*, further research might be required in certain aspects of the present invention, this does not preclude a finding that the invention has utility, as set forth by the Federal Circuit's holding in *Brana*, which clearly states, as highlighted in the quote above, that "pharmaceutical inventions, necessarily includes the expectation of further research and development" (*Brana* at 1442-1443, emphasis added). In assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In re Angstadt and Griffin*, 190 USPQ 214 (CCPA 1976). The need for some experimentation does not render the claimed invention unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988).

It is important to note that it has been clearly established that a statement of utility in a specification must be accepted absent reasons why one skilled in the art would have reason to doubt the objective truth of such statement. *In re Langer*, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA, 1974; "*Langer*"); *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA, 1971). As clearly set forth in *Langer*:

> As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as sufficient to satisfy the utility requirement of § 101 for the entire claimed subject matter unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope.

Langer at 297, emphasis in original. As set forth in the MPEP, "Office personnel must provide evidence sufficient to show that the statement of asserted utility would be considered 'false' by a person of ordinary skill in the art" (MPEP, Eighth Edition at 2100-40, emphasis added). Absent such evidence from the Examiner, as the skilled artisan would readily understand that the

present polymorphic markers have utility in forensic analysis, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Although Applicants need only make one credible assertion of utility to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), Applicants point out that the presently claimed sequence shares nearly 100% identity over the entire length of the claimed sequence with a sequence that is present in the leading scientific repository for biological sequence data (GenBank), and which has been annotated by third party scientists *wholly unaffiliated with Applicants* as "*Homo sapiens* oviductin protease" (GenBank accession number NM_198185; alignment and GenBank report provided in **Exhibit A**). Importantly, although the sequence presented in NM_198185 is longer than the claimed sequence, the trypsin-like serine protease domain identified in the NM_198185 GenBank report is present in the claimed sequence. Furthermore, the presently claimed sequence also shares nearly 100% identity over the entire length of the claimed sequence with two additional sequences that haves been annotated by third party scientists *wholly unaffiliated with Applicants* as "*Homo sapiens* serine protease CVSP14" (Published PCT Patent Application Number WO 02/77263; alignment and WIPO printout provided in **Exhibit B**) and "*Homo sapiens* protease PRTS-20" (Published PCT Patent Application Number WO 01/98468; alignment and WIPO printout provided in **Exhibit C**). The legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. Given this GenBank annotation, and the annotations in the published PCT Patent Applications, there can be no question that those skilled in the art would clearly believe that Applicants' sequence is a trypsin-like protease, such as oviductin, exactly as asserted by Applicants in the specification as originally filed (see, at least, page 2, lines 1-2). Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

Thus, the present situation appears to track Example 10 of the Revised Interim Utility Guidelines Training Materials (pages 53-55; **Exhibit D**), which clearly establishes that a rejection under 35 U.S.C. § 101 as allegedly lacking a patentable utility and under 35 U.S.C. § 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility (see Section VI, below), is not proper when a full length sequence (such as the presently claimed sequence), and has a similarity score greater than 95% to a protein having a known function (such as the nearly 100% identity between the presently claimed

sequence and the oviductin protease sequence, as discussed above). Therefore, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

Therefore, as just one example of the utility of the present nucleotide sequences, the skilled artisan would readily appreciate the utility of tracking expression of the presently claimed sequence. The specification details, at least at page 5, lines 11-14, that the present nucleotide sequences have utility in assessing gene expression patterns using high-throughput DNA chips. Such "DNA chips" clearly have utility, as evidenced by hundreds of issued U.S. Patents, as exemplified by U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, 5,837,832, 6,156,501 and 6,261,776. As the present sequences are specific markers of human chromosome 11 (see below), and such specific markers are targets for the discovery of drugs that are associated with human disease, those of skill in the art would instantly recognize that the present nucleotide sequences would be an ideal, novel candidate for assessing gene expression using such DNA chips. Given the widespread utility of such "gene chip" methods using *public domain* gene sequence information, there can be little doubt that the use of the presently described *novel* sequences would have great utility in such DNA chip applications. Clearly, compositions that enhance the utility of such DNA chips, such as the presently claimed nucleotide sequences, must in themselves be useful.

Evidence of the "real world" substantial utility of the present invention is further provided by the fact that there is an entire industry established based on the use of gene sequences or fragments thereof in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies which have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, one such company (Rosetta Inpharmatics) was viewed to have such "real world" value that it was acquired by large a pharmaceutical company (Merck) for significant sums of money (net equity value of the transaction was $620 million). The "real world" substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. Clearly, persons of skill in the art, as well as venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. Billions of dollars have been invested in the human genome project, resulting in useful genomic data (see, *e.g.*, Venter *et al.*, 2001, Science *291*:1304). The results have been a stunning success as the utility of human genomic data has been widely recognized as a great gift to humanity (see, *e.g.*, Jasny and Kennedy, 2001, Science *291*:1153). Clearly, the usefulness of human genomic

data, such as the presently claimed nucleic acid molecules, is substantial and credible (worthy of billions of dollars and the creation of numerous companies focused on such information) and well-established (the utility of human genomic information has been clearly understood for many years). Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

The Examiner also discounts this asserted utility, stating that this utility "is an application which (*sic*) would apply to every member of a general class of materials and/or is a use only for further research to determine a use for SEQ ID NO:1 or the protein encoded thereby" (Action bridging pages 2 and 3). Applicants point out that only expressed sequences can be used to track gene expression, not just any nucleic acid. Expression profiling does not require a knowledge of the function of the particular nucleic acid on the chip - rather the gene chip indicates which DNA fragments are expressed at greater or lesser levels in two or more particular tissue types. Skilled artisans already have used and continue to use sequences such as Applicants in gene chip applications without further experimentation. Furthermore, the fact that other nucleotide sequences can be used to track gene expression would not mean that the use of Applicants' sequence to track gene expression is not a specific utility (*Carl Zeiss Stiftung v. Renishaw PLC*, *supra*). Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

As yet a further example of the utility of the presently claimed polynucleotide, as described in the specification at least at page 10, line 19, the present nucleotide sequence has a specific utility in "determining the genomic structure". Alignment of SEQ ID NO:1 with GenBank accession number AC104237 (a genomic clone from human chromosome 11) shows that the human gene corresponding to the presently claimed sequence is dispersed on 7 exons of human chromosome 11 (alignment and first page of the GenBank report are presented in **Exhibit E**). Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of human chromosome 11 that contains the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence. For further evidence in support of the Applicants' position, the Examiner is requested to review, for example, section 3 of Venter *et al.* (*supra*, at pp. 1317-1321, including Fig. 11 at pp.1324-1325), which demonstrates the

significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter *et al.* article. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

The Examiner also discounts this asserted utility, stating that this utility "is an application which (*sic*) would apply to every member of a general class of materials and/or is a use only for further research to determine a use for SEQ ID NO:1 or the protein encoded thereby" (Action bridging pages 2 and 3). Applicants respectfully remind the Examiner that only a minor percentage (2-4%) of the genome actually encodes exons, which in-turn encode amino acid sequences. Equally significant is that the claimed polynucleotide sequence defines how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). Applicants point out that the claimed sequences identify biologically verified exon splice junctions, as opposed to splice junctions that may have been bioinformatically predicted from genomic sequence alone. The specification details that "sequences derived from regions adjacent to the intron/exon boundaries of the human gene can be used to design primers for use in amplification assays to detect mutations within the exons, introns, splice sites (*e.g.*, splice acceptor and/or donor sites), *etc.*, that can be used in diagnostics and pharmacogenomics" (specification at page 10, lines 20-25). Applicants respectfully submit that the practical scientific value of biologically validated, expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts. Additionally, the fact that other nucleotide sequences can be used to identify exon splice junctions and map this specific region of human chromosome 11 does not mean that these uses of Applicants' sequence are not specific utilities (*Carl Zeiss Stiftung v. Renishaw PLC, supra*). Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

Rather, as set forth by the Federal Circuit, "(t)he threshold of utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip Inc. v. Orange Bang Inc.*, 51 USPQ2d 1700 (Fed. Cir. 1999) (citing *Brenner v. Manson*, 383 U.S. 519, 534 (1966)). Additionally, the Federal Circuit has stated that "(t)o violate § 101 the claimed device must be totally incapable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 (Fed. Cir. 1992), emphasis added. *Cross v. Iizuka* (224 USPQ 739 (Fed. Cir. 1985); "*Cross*") states "any utility of the claimed compounds is sufficient to satisfy 35 U.S.C. § 101". *Cross* at 748, emphasis added. Indeed, the Federal

Circuit recently emphatically confirmed that "anything under the sun that is made by man" is patentable *(State Street Bank & Trust Co. v. Signature Financial Group Inc.*, 47 USPQ2d 1596, 1600 (Fed. Cir. 1998), citing the U.S. Supreme Court's decision in *Diamond vs. Chakrabarty*, 206 USPQ 193 (S.Ct. 1980)).

Finally, the requirements set forth in the Action for compliance with 35 U.S.C. § 101 do not comply with the requirements set forth by the Patent and Trademark Office ("the PTO") itself for compliance with 35 U.S.C. § 101. While Applicants are well aware of the new Utility Guidelines set forth by the USPTO, Applicants respectfully point out that the current rules and regulations regarding the examination of patent applications is and always has been the patent laws as set forth in 35 U.S.C. and the patent rules as set forth in 37 C.F.R., not the Manual of Patent Examination Procedure or particular guidelines for patent examination set forth by the USPTO. Furthermore, it is the job of the judiciary, not the USPTO, to interpret these laws and rules. Applicants are unaware of any significant recent changes in either 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit that is in keeping with the new Utility Guidelines set forth by the USPTO. This is underscored by numerous patents that have been issued over the years that claim nucleic acid fragments that do not comply with the new Utility Guidelines. As examples of such issued U.S. Patents, the Examiner is invited to review U.S. Patent Nos. 5,817,479, 5,654,173, and 5,552,281 (each of which claims short polynucleotides), and recently issued U.S. Patent No. 6,340,583 (which includes no working examples), none of which contain examples of the "real-world" utilities that the Examiner seems to be requiring. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section VII, below), Applicants submit that the present polynucleotides must also meet the requirements of 35 U.S.C. § 101. While Applicants understand that each application is examined on its own merits, Applicants are unaware of any changes to 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit, since the issuance of these patents that render the subject matter claimed in these patents, which is similar to the subject matter in question in the present application, as suddenly non-statutory or failing to meet the requirements of 35 U.S.C. § 101. Thus, holding Applicants to a different standard of utility would be arbitrary and capricious, and, like other clear violations of due process, cannot stand.

For each of the foregoing reasons, Applicants submit that as the presently claimed nucleic acid molecules have been shown to have a substantial, specific, credible and well-established utility, the rejection of claims 1-3 under 35 U.S.C. § 101 has been overcome, and request that the

rejection be withdrawn.

VI. Rejection of Claim 2 Under 35 U.S.C. § 112, Second Paragraph

The Action next rejects claim 2 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the invention.

The Action rejects claim 2 as allegedly indefinite based on the term "stringent hybridization conditions", because the specific hybridization and washing conditions are not recited in the claim. Applicants stress that "a claim need not 'describe' the invention, such description being the role of the disclosure". *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986). However, while Applicants submit that the term is sufficiently definite, as a number of stringent hybridization conditions are defined in the specification and would be known to those of skill in the art, solely in order to progress the case more rapidly toward allowance the claim has been revised to recite specific highly stringent hybridization conditions. As the specification provides specific teaching regarding such highly stringent hybridization conditions, at least at page 4, lines 4-7, Applicants submit that revised claim 2 even more clearly meets the requirements of 35 U.S.C. § 112, second paragraph. Applicants therefore request withdrawal of this rejection.

VII. Rejection of Claims 1-3 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claims 1-3 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by a specific, substantial, and credible utility or a well-established utility. Applicants respectfully traverse.

Applicants submit that as claims 1-3 have been shown to have "a specific, substantial, and credible utility", as detailed in section V above, the present rejection of claims 1-3 under 35 U.S.C. § 112, first paragraph, cannot stand.

Applicants therefore request that the rejection of claims 1-3 under 35 U.S.C. § 112, first paragraph, be withdrawn.

VIII. Rejection of Claim 1 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claim 1 under 35 U.S.C. § 112, first paragraph, as allegedly not providing enablement for the full scope of the claimed invention comprising a genus of at least 24 contiguous nucleotides of SEQ ID NO:1. Applicants respectfully traverse.

The Action states that claim 1 is not enabled because the specification does not establish "(A) regions of the protein structure encoded by SEQ ID NO:1 which may be modified without effecting the activity; (B) the general tolerance of said activity to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful" (Action bridging pages 5 and 6). Applicants point out that the above comments are completely irrelevant to determining whether the claimed compositions meet the legal requirements for patentability under 35 U.S.C. § 112, first paragraph. There is absolutely **no** requirement that all species of an invention must have all of the exact same properties. It is well established that the enablement requirement is met if **any** use of the invention (or in this case, certain species of the invention) is provided (*In re Nelson*, 126 USPQ 242 (CCPA 1960); *Cross v. Iizuka, supra*). "The enablement requirement is met if the description enables any mode of making and using the invention." *Johns Hopkins Univ. v. CellPro, Inc.*, 47 USPQ2d 1705, 1719 (Fed. Cir. 1998), citing *Engel Indus., Inc. v. Lockformer Co.*, 20 USPQ2d 1300, 1304 (Fed. Cir. 1991). Enablement only requires that the specification describe a practical use for the composition defined in the claims, and that a skilled artisan be able to make and use the claimed DNA segments without undue experimentation. Accordingly, the § 112 requirement has certainly been met.

The Action seems to contend that the specification provides insufficient guidance regarding the biological function or activity of certain of the claimed compositions. However, such an enablement standard conflicts with established patent law. As discussed *In re Brana, supra*, the Federal Circuit admonished the P.T.O. for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442.

The Examiner cites *In re Wands* (*supra*) for the proposition that the present invention could not be practiced without "undue experimentation". However, it is important to remember that in assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In re Angstadt and Griffin, supra.* In *Wands*, the P.T.O. took the position that the applicant failed to demonstrate that the disclosed biological processes of immunization and antibody selection could reproducibly result in a useful biological product (antibodies from hybridomas) within the scope of the claims. In its decision overturning the P.T.O.'s rejection, the Federal Circuit found that

Wands' demonstration of success in four out of nine cell lines screened was sufficient to support a conclusion of enablement. The court emphasized that the need for some experimentation requiring, *e.g.*, production of the biological material followed by routine screening, was not a basis for a finding of non-enablement, stating:

> Disclosure in application for the immunoassay method patent does not fail to meet enablement requirement of 35 USC 112 by requiring 'undue experimentation,' even though production of monoclonal antibodies necessary to practice invention first requires production and screening of numerous antibody producing cells or 'hybridomas,' since practitioners of art are prepared to screen negative hybridomas in order to find those that produce desired antibodies, since in monoclonal antibody art one 'experiment' is not simply screening of one hybridoma but rather is entire attempt to make desired antibody, and since record indicates that amount of effort needed to obtain desired antibodies is not excessive, in view of Applicants' success in each attempt to produce antibody that satisfied all claim limitations.

Wands at 1400. Thus, the need for some experimentation does not render the claimed invention unpatentable under 35 U.S.C. § 112, first paragraph. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd., supra.*

Applicants point out that significant commercial exploitation of nucleic acid sequences requires no more information than the nucleic acid sequence itself. Applications ranging from gene expression analysis or profiling (utilizing, for example, arrays of short, overlapping or non-overlapping, oligonucleotides and DNA chips, as described in Section V, above) to chromosomal mapping (utilizing, for example, short oligonucleotide probes or full length DNA sequences, as described in Section V, above) are practiced utilizing nucleic acid sequences and techniques that are well-known to those of skill in the art. The widespread commercial exploitation of nucleic acid sequence information points to the level of skill in the art, and the enablement provided by disclosures such as the present specification, which include specific nucleic acid sequences and guidance regarding the various uses of such sequences.

The Action questions the teaching and guidance in the specification for certain aspects of the present invention. However, as discussed above, this requirement is completely misplaced. There is sufficient knowledge and technical skill in the art for a skilled artisan to be able to make and use the claimed DNA species in a number of different aspects of the invention entirely without further details in a patent specification. For example, it is not unreasonable to expect a Ph.D. level molecular biologist to be able to use the disclosed sequence to design oligonucleotide probes and primers and use them in, for example, PCR based screening and detection methods

to obtain the described sequences and/or determine tissue expression patterns. Nevertheless, the present specification provides highly detailed descriptions of techniques that can be used to accomplish many different aspects of the claimed invention, including recombinant expression, site-specific mutagenesis, *in situ* hybridization, and large scale nucleic acid screening techniques, and properly incorporates by reference a montage of standard texts into the specification, such as Sambrook *et al.* (*Molecular Cloning, A Laboratory Manual*) and Ausubel *et al.* (*Current Protocols in Molecular Biology*) to provide even further guidance to the skilled artisan. Incorporation of material into the specification by reference is proper. *Ex parte Schwarze*, 151 USPQ 426 (PTO Bd. App. 1966). The § 112, first paragraph rejection is thus *prima facie* improper:

> As a matter of patent office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

In re Marzocchi, supra, emphasis as in original. In any event, an alleged lack of express teaching is insufficient to support a first paragraph rejection where one of skill in the art would know how to perform techniques required to perform at least one aspect of the invention. As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands, supra*. In fact, it is preferable that what is well known in the art be omitted from the disclosure. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81 (Fed. Cir. 1986). As standard molecular biological techniques are routine in the art, such protocols do not need to described in detail in the specification.

Furthermore, a specification "need describe the invention only in such detail as to enable a person skilled in the most relevant art to make and use it." *In re Naquin*, 158 USPQ 317, 319 (CCPA 1968); emphasis added. The present claims are thus enabled as they are supported by a specification that provides sufficient description to enable the skilled person to make and use the invention as claimed.

As detailed above, and in the previous response, all aspects of the enablement rejection under 35 U.S.C. § 112, first paragraph have been overcome. Applicants therefore respectfully request that the rejection be withdrawn.

IX. Rejection of Claim 1 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claim 1 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse.

35 U.S.C. § 112, first paragraph, requires that the specification contain a written description of the invention. The Federal Circuit in *Vas-Cath Inc. v. Mahurkar* (19 USPQ2d 1111 (Fed. Cir. 1991); "*Vas-Cath*") held that an "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.*" *Vas-Cath*, at 1117, emphasis in original. However, it is important to note that the above finding uses the terms reasonable clarity to those skilled in the art. Further, the Federal Circuit in *In re Gosteli* (10 USPQ2d 1614 (Fed. Cir. 1989); "*Gosteli*") held:

> Although [the applicant] does not have to describe exactly the subject matter claimed, . . . the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.

Gosteli at 1618, emphasis added. Additionally, *Utter v. Hiraga* (6 USPQ2d 1709 (Fed. Cir. 1988); "*Utter*"), held "(a) specification may, within the meaning of 35 U.S.C. § 112 ¶1, contain a written description of a broadly claimed invention without describing all species that claim encompasses" (*Utter*, at 1714). Therefore, all Applicants must do to comply with 35 U.S.C. § 112, first paragraph, is to convey the invention with reasonable clarity to the skilled artisan.

Further, the Federal Circuit has held that an adequate description of a chemical genus "requires a precise definition, such as by structure, formula, chemical name or physical properties" sufficient to distinguish the genus from other materials. *Fiers v. Sugano*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993; "*Fiers*"). *Fiers* goes on to hold that the "application satisfies the written description requirement since it sets forth the . . . nucleotide sequence" (*Fiers* at 1607). In other words, provision of a structure and formula - the nucleotide sequence - renders the application in compliance with 35 U.S.C. § 112, first paragraph.

More recently, the standard for complying with the written description requirement in claims involving chemical materials has been explicitly set forth by the Federal Circuit:

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. *Regents of Univ. of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Thus, a claim describing a genus of nucleic acids by structure, formula, chemical name or physical properties sufficient to allow one of ordinary skill in the art to distinguish the genus from other materials meets the written description requirement of 35 U.S.C. § 112, first paragraph. As further elaborated by the Federal Circuit in *Regents of Univ. of California v. Eli Lilly and Co.*:

> In claims to genetic material ... a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA', without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art cannot, as one can do with a fully described genus, visualize or recognize the identity of members of the genus. (Emphasis added)

Thus, as opposed to the situation set forth in *Regents of Univ. of California v. Eli Lilly and Co.* and *Fiers*, the nucleic acid sequences of the present invention are not distinguished on the basis of function, or a method of isolation, but in fact are distinguished by structural features - a chemical formula, *i.e.*, the *sequence itself.*

Using the nucleic acid and amino acid sequences of the present invention (as set forth in the Sequence Listing), the skilled artisan would readily be able to distinguish the claimed nucleic acids from other materials on the basis of the specific structural description provided. Polynucleotides that comprise at least 34 contiguous nucleotides from SEQ ID NO:1 are within the genus of the instant claims, while those that lack this structural feature lie outside the genus. Claim 1 thus meets the written description requirement.

For each of the foregoing reasons, Applicants submit that the rejection of claim 1 under 35 U.S.C. § 112, first paragraph, has been overcome, and request that the rejection be withdrawn.

X. Rejection of Claim 1 Under 35 U.S.C. § 102(b)

The Action next rejects claim 1 under 35 U.S.C. § 102(b), as allegedly anticipated by Yu *et al.* (*J. Biol. Chem.* **270**:13483-13489, 1995; "Yu"). While Applicants do not necessarily agree with the present rejection, as claim 1 has been amended to recite an isolated nucleic acid molecule comprising at least 34 contiguous nucleotides from SEQ ID NO:1, which is neither taught nor suggested by Yu, Applicants submit that the rejection of claim 1 under 35 U.S.C. § 102(b) has been overcome.

Applicants therefore respectfully request that the rejection of claim 1 under 35 U.S.C. § 102(b) be withdrawn.

XI. Rejection of Claim 1 Under 35 U.S.C. § 102(b)

The Action next rejects claim 1 under 35 U.S.C. § 102(b), as allegedly anticipated by Shibuya *et al.* (*Biochim. Biophys. Acta* **1206**:63-70, 1994; "Shibuya"). While Applicants do not necessarily agree with the present rejection, as claim 1 has been amended to recite an isolated nucleic acid molecule comprising at least 34 contiguous nucleotides from SEQ ID NO:1, which is neither taught nor suggested by Shibuya, Applicants submit that the rejection of claim 1 under 35 U.S.C. § 102(b) has been overcome.

Applicants therefore respectfully request that the rejection of claim 1 under 35 U.S.C. § 102(b) be withdrawn.

XII. Rejection of Claim 1 Under 35 U.S.C. § 102(e)

The Action next rejects claim 1 under 35 U.S.C. § 102(e), as allegedly anticipated by Ashkenazi *et al.* (U.S. Patent Application Publication Number 20030004102; "Ashkenazi"). While Applicants do not necessarily agree with the present rejection, as claim 1 has been amended to recite an isolated nucleic acid molecule comprising at least 34 contiguous nucleotides from SEQ ID NO:1, which is neither taught nor suggested by Ashkenazi, Applicants submit that the rejection of claim 1 under 35 U.S.C. § 102(e) has been overcome.

Applicants therefore respectfully request that the rejection of claim 1 under 35 U.S.C. § 102(e) be withdrawn.

XIII. Rejection of Claim 1 Under 35 U.S.C. § 102(e)

The Action next rejects claim 1 under 35 U.S.C. § 102(e), as allegedly anticipated by Wu-Hunter *et al.* (U.S. Patent Number 6,210,920; "Wu-Hunter"). While Applicants do not necessarily agree with the present rejection, as claim 1 has been amended to recite an isolated nucleic acid molecule comprising at least 34 contiguous nucleotides from SEQ ID NO:1, which is neither taught nor suggested by Wu-Hunter, Applicants submit that the rejection of claim 1 under 35 U.S.C. § 102(e) has been overcome.

Applicants therefore respectfully request that the rejection of claim 1 under 35 U.S.C. § 102(e) be withdrawn.

XIV. Rejection of Claim 1 Under 35 U.S.C. § 102(a)

The Action next rejects claim 1 under 35 U.S.C. § 102(a), as allegedly anticipated by Wood *et al.* (PCT Patent Application Number WO 99/46281; "Wood"). While Applicants do

not necessarily agree with the present rejection, as claim 1 has been amended to recite an isolated nucleic acid molecule comprising at least 34 contiguous nucleotides from SEQ ID NO:1, which is neither taught nor suggested by Wood, Applicants submit that the rejection of claim 1 under 35 U.S.C. § 102(a) has been overcome.

Applicants therefore respectfully request that the rejection of claim 1 under 35 U.S.C. § 102(a) be withdrawn.

XV. Conclusion

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Swope have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

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